

WHAT IS CLAIMED IS:

1. A pharmaceutical composition for administration to a subject mammal exhibiting a diurnal cycle of plasma aldosterone concentration having an acrophase, the composition comprising a therapeutically effective amount of a delayed-release formulation of an aldosterone antagonist drug which, when orally administered about 6 to about 12 hours prior to the acrophase, provides a profile of plasma drug concentration corresponding substantially to the diurnal cycle of plasma aldosterone concentration.
2. The composition of Claim 1 wherein the profile of plasma drug concentration corresponds to the diurnal cycle of plasma aldosterone concentration substantially as depicted in Fig. 1. *omnibus*
3. A pharmaceutical composition comprising a delayed-release formulation of an aldosterone antagonist drug in a therapeutically effective amount, the composition exhibiting a release profile, as determined by a suitable test, in which:
- (a) zero to about 20% by weight of the drug is released from the formulation at about 4 hours after initiation of the test; and
- (b) about 50% to 100% by weight of the drug is released from the formulation within a time period of about 3 hours beginning at a time about 4 to about 12 hours after initiation of the test. *50-100% released in 3hrs after 4hr delay*
4. The composition of Claim 3 wherein the test is conducted according to U.S. Pharmacopeia 24, Test No. 711, using apparatus 2 at 50 rpm, with an aqueous dissolution medium containing 1% sodium dodecyl sulfate at 37°C, and wherein release is measured by dissolution of the drug in the medium.
5. The composition of Claim 3 wherein zero to about 10% by weight of the drug is released from the formulation at about 4 hours after initiation of the test.
6. The composition of Claim 3 wherein zero to about 20% by weight of the drug is released from the formulation at about 6 hours after initiation of the test.
7. The composition of Claim 3 wherein zero to about 10% by weight of the drug is released from the formulation at about 6 hours after initiation of the test.

8. The composition of Claim 3 wherein about 70% to 100% by weight of the drug is released from the formulation within said time period of about 3 hours.
9. The composition of Claim 1 that further comprises a second formulation comprising a therapeutically effective amount of a second antihypertensive agent.
10. The composition of Claim 9 wherein said second antihypertensive agent is selected from a diuretic, a sympatholytic agent, an ACE inhibitor, a vasopectidase, a calcium channel blocker, a direct vasodilator, a renin inhibitor, and an angiotensin II antagonist.
- 10 11. The composition of Claim 9 wherein the second formulation containing the second antihypertensive agent exhibits a release profile that is different from the release profile exhibited by the delayed-release formulation containing the aldosterone antagonist.
12. The composition of Claim 11 wherein the second formulation is an immediate-release formulation.
- 15 13. The composition of Claim 11 wherein the second formulation is an extended-release formulation.
14. The composition of Claim 1 wherein the aldosterone antagonist is eplerenone.
15. The composition of Claim 1 that is in the form of an enteric coated tablet.
- 20 16. The composition of Claim 15 wherein the tablet comprises a core comprising an immediate-release formulation of the aldosterone antagonist substantially enclosed within an enteric coating.
17. The composition of Claim 1 that is in the form of a capsule containing enteric coated pellets.
- 25 18. The composition of Claim 17 wherein the pellets each comprise a core comprising an immediate-release formulation of the aldosterone antagonist substantially enclosed within an enteric coating.
19. A method of treating a mammal exhibiting (a) circadian rhythm in aldosterone secretion having an acrophase and (b) an aldosterone-mediated disease or

C-3318/1/US

disorder, the method comprising orally administering to the mammal a composition of any of Claims 1-18 about 6 to about 12 hours prior to the acrophase.

20. The method of Claim 19 wherein the mammal is a human.
- 5 21. The method of Claim 20 wherein the disease or disorder is elevated blood pressure.
22. The method of Claim 20 wherein the acrophase occurs at the end of a sleep period and the composition is orally administered prior to the sleep period.

09551264 051101

add
B1